

Amendments to the Claims

The following listing of claims replaces all prior versions and listings of claims in this application:

Claims 1-30. (Cancelled)

31. (Currently amended) A pharmaceutical composition for bone elongation or treating skeletal dysplasias comprising at least one natriuretic peptide variant, or variants thereof the peptide being set forth in SEQ ID NO:5 wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; and Xgg=Leu, Met, and a carrier or excipient, wherein SEQ ID NO:5 is other than amino acid sequence set forth in SEQ ID NO:2.

32. (Cancelled)

33. (Cancelled)

34. (Withdrawn) The pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is according to any one of SEQ ID Nos: 1-4.

35. (Withdrawn) The pharmaceutical composition according to claim 34 wherein said at least one natriuretic peptide is a BNP.

36. (Original) The pharmaceutical composition according to claim 31 further comprising an inhibitor of the natriuretic peptide clearance receptor.

37. (Original) The pharmaceutical composition according to claim 31 further comprising an inhibitor of the neutral endopeptidase 24.11.

38. (Original) The pharmaceutical composition according to claim 37 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

39. (Currently amended) The pharmaceutical composition according to claim 31 further comprising an inhibitor of fibroblast growth factor receptor 3 tyrosine kinase.

40. (Currently amended) ~~[[The]] A pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is a~~ comprising a natriuretic peptide fused to a carrier

protein forming a natriuretic peptide-carrier protein fusion protein, wherein the carrier protein is a bone growth plate-specific protein.

41. (Original) The pharmaceutical composition according to claim 40 wherein the carrier protein comprises growth hormone.

42. (Currently amended) The pharmaceutical composition according to claim 40 [[31]] wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

43. (Cancelled)

44. (Cancelled)

45. (Withdrawn) A method for treatment of skeletal dysplasias comprising the step of administering to a patient a therapeutically effective amount of at least one natriuretic peptide in a pharmaceutical composition according to claim 31.

46. (Withdrawn) The method according to claim 45 wherein said at least one natriuretic peptide is a CNP.

47. (Withdrawn) The method according to claim 45 wherein said at least one natriuretic peptide is a CNP variant according to SEQ ID NO:5 having amino acid sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.

48. (Withdrawn) The method according to claim 45 wherein said at least one natriuretic peptide is according to any one of SEQ ID NOs:1-4.

49. (Withdrawn) The method according to claim 48 wherein said at least one natriuretic peptide is a BNP.

50. (Withdrawn) The method according to claim 45 further comprising inhibiting the natriuretic peptide clearance receptor.

51. (Withdrawn) The method according to claim 45 further comprising an inhibitor of neutral endopeptidase 24.11 with an inhibitor.

52. (Withdrawn) The method according to claim 49 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

53. (Withdrawn) The method according to claim 45 wherein the step of administering to the patient an inhibitor of neutral endopeptidase 24.11 is performed simultaneously with the step of administering to a patient an effective amount of at least one natriuretic peptide.

54. (Withdrawn) The method according to claim 45 further comprising administering to the patient an inhibitor of tyrosine kinase.

55. (Withdrawn) The method according to claim 45 wherein said at least one natriuretic peptide is a natriuretic peptide fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

56. (Withdrawn) The method according to claim 55 wherein the carrier protein fusion protein comprises growth hormone.

57. (Withdrawn) The method according to claim 45 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

58. (Withdrawn) The method according to claim 45 wherein the bone is a limb bone.

59. (Withdrawn) The method according to claim 58 wherein the limb bone is an achondroplasiac bone.

Claims 60 - 66. (Cancelled)

67. (Withdrawn) A method for increasing the size of a bone growth plate in abnormal bone comprising treating the bone with an effective amount of at least one natriuretic peptide in a pharmaceutical composition according to claim 31.

68. (Withdrawn) The method according to claim 67 wherein said at least one natriuretic peptide is a CNP.

69. (Withdrawn) The method according to claim 67 wherein said at least one natriuretic peptide is a CNP variant according to SEQ ID NO:5 having amino acid sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.

70. (Withdrawn) The method according to claim 67 wherein said at least one natriuretic peptide is according to any one of SEQ ID NOs:1-4.

71. (Withdrawn) The method according to claim 70 wherein said at least one natriuretic peptide is a BNP.

72. (Withdrawn) The method according to claim 67 further comprising inhibiting the natriuretic peptide clearance receptor.

73. (Withdrawn) The method according to claim 67 further comprising an inhibitor of the neutral endopeptidase 24.11.

74. (Withdrawn) The method according to claim 73 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

75. (Withdrawn) The method according to claim 74 wherein the step of administering an inhibitor of neutral endopeptidase is performed simultaneously with the step of administering an effective amount of at least one natriuretic peptide.

76. (Withdrawn) The method according to claim 67 further comprising an inhibitor of tyrosine kinase.

77. (Withdrawn) The method according to claim 68 wherein said at least one natriuretic peptide is fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

78. (Withdrawn) The method according to claim 77 wherein the carrier protein fusion protein comprises growth hormone.

79. (Withdrawn) The method according to claim 67 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.
80. (Withdrawn) The method according to claim 67 wherein the bone is a limb bone.
81. (Withdrawn) The method according to claim 80 wherein the limb bone is an achondroplastic bone.
82. (Withdrawn) A method for elongation of an abnormal bone, comprising treating the bone with an effective amount of at least one natriuretic peptide in a pharmaceutical composition according to claim 31.
83. (Withdrawn) The method according to claim 82 wherein said at least one natriuretic peptide is a CNP.
84. (Withdrawn) The method according to claim 82 wherein said at least one natriuretic peptide is a CNP variant according to SEQ ID NO:5 having amino acid sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.
85. (Withdrawn) The method according to claim 82 wherein said at least one natriuretic peptide is according to any one of SEQ ID NOs:1-4.
86. (Withdrawn) The method according to claim 85 wherein said at least one natriuretic peptide is a BNP.
87. (Withdrawn) The method according to claim 82 further comprising inhibiting the natriuretic peptide clearance receptor.
88. (Withdrawn) The method according to claim 82 further comprising an inhibitor of the neutral endopeptidase 24.11.

89. (Withdrawn) The method according to claim 88 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

90. (Withdrawn) The method according to claim 88 wherein the step of administering an inhibitor of neutral endopeptidase is performed simultaneously with the step of administering an effective amount of at least one natriuretic peptide.

91. (Withdrawn) The method according to claim 82 further comprising an inhibitor of tyrosine kinase.

92. (Withdrawn) The method according to claim 82 wherein said at least one natriuretic peptide is a natriuretic peptide fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

93. (Withdrawn) The method according to claim 92 wherein the carrier protein comprises growth hormone.

94. (Withdrawn) The method according to claim 82 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

95. (Withdrawn) The method according to claim 82 wherein the bone is a limb bone.

96. (Withdrawn) The method according to claim 82 wherein the limb bone is an achondroplastic bone.